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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/924,011	08/07/2001	John R. DePhillipo	E0543-00011	1968

8933 7590 06/17/2005

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EXAMINER	
KAUSHAL, SUMESH	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/924,011	DEPHILLIPO ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-9,11,12,14-27,30-36 and 57-62* is/are pending in the application.

4a) Of the above claim(s) *11,12,34-36,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-9, 14-27, 30-33 and 59-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 4/11/05 has been acknowledged.

Claims 2-5, 10, 13, 28-29, 37-56, are canceled.

Claims 1, 6-9, 11-12, 14-27, 30-36 and 57-62 are pending

Claims 11-12, 34-36, 57-58 are withdrawn.

Claims 1, 6-9, 14-27, 30-33 and 59-62 are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***571-273-8300.***

Election/Restrictions

Applicant's election with traverse of VI in the reply filed on 04/11/05 is acknowledged. The traversal is on the ground(s) that group VI and IX should be joined together. This is found persuasive. Group VI and IX are joined together, wherein the elected combination of two disorder-associated polymorphism (DAP) is gene encoding Vitamin D receptor and Interleukin-6, wherein the Vitamin D receptor DAP comprises occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor, wherein the Interleukin-6 DAP comprises occurrence of a cytosine residue at position -1 74 of the interleukin 6 gene promoter;

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 6-7, 14-27 and 30-32 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of instant claim encompass a method of assessing relative susceptibility of a human to an undesirable bone density condition that requires the identification of any two disorder-associated polymorphism associated with transmembrane signaling pathway and bone resorption. The scope of invention as claimed encompasses a huge genre of genes involved in transmembrane signaling pathway and bone resorption. At best the specification discloses Vitamin D receptor and Interleukin-6 related single nucleotide polymorphism that falls in the scope of instant invention.

Applicant is referred to the guidelines for *Written Description Requirement* published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov). The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In analyzing whether the written description requirement is met for the genus claim, it is first determined whether a representative number of species have been described by their complete

structure. In the instant case, the specification does not provide a common structure that represents any and all transmembrane signaling pathway genes and any and all bone resorption genes. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. Since specification fails to disclose any common structure for the claimed genes, it is not possible to envision the claimed compositions for it's full scope. Therefore, the limited disclosure in the specification is not deemed sufficient to reasonably convey to one skilled in the art that the applicants were in possessions of the huge genera recited in the claims at the time the application was filed. The specification fails to define the minimal structure or consensus core structure that defines the genus comprising nucleotide sequences encoding any transmembrane signaling pathway and bone resorption gene that modulates bone density.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by

function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).* In the instant case the DAP genes as claimed has been defined only by a statement of function that broadly encompasses any transmembrane signaling pathway activity and bone resorption activity, which conveyed no distinguishing information about the identity of the DAP gene sequence, such as its relevant structural or physical characteristics. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Claims 1, 6-9, 14-27, 30-33 and 59-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Nature Of Invention:

Invention relates to a method for diagnosing an undesirable bone density condition using combination of single nucleotide polymorphism (SNP) from unrelated genes.

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of instant claim encompass a method of assessing relative susceptibility of a human to an undesirable bone density condition that requires the identification of any two disorder-associated polymorphism associated with transmembrane signaling pathway and bone resorption. The scope of invention as claimed encompasses a huge genre of genes involved in transmembrane signaling pathway and bone resorption. The specification as filed fails to disclose that assessing the polymorphisms in any transmembrane signaling pathway gene along with any bone resorption gene is significantly predictive of diagnosing any undesirable bone density condition (i.e. osteophorosis or high bone mass). The specification even fails to establish any bone density condition (i.e. osteophorosis or high bone mass) is associated with any and all polymorphic genes associated with Vitamin D receptor and Interleukin-6 genes. The specification even fails to provide any evidence that establishes the association of any undesirable bone density condition (like osteophorosis or high bone mass) is associated with the occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor and a cytosine residue at position -174 of the interleukin-6 gene promoter. Considering the instant specification it is even unclear how bone density is affected by the presence of these SNPs in a human. In addition the specification fails to provide any evidence (linkage analysis for candidate genes), which establishes that assessment of these SNPs in combination would be a better predictor of assessing an undesirable bone density as compared to identification of any single SNP.

State Of Art And Predictability:

The state of the art at the time of filing teaches that osteoporosis is a common disorder with a complex patho-physiology involving both endogenous and environmental factors. The family and twin studies have shown that genetic factors play an essential role in bone mass regulation and that apart from rare instances the heritability of bone mineral density and osteoporosis is polygenic. An important problem with most candidate gene studies is small sample size, and this has led to conflicting results in different populations. Even though candidate gene association studies are relatively easy to perform, the disadvantages include the possibility of false positive (or false negative) results due to confounding factors and population stratification. Furthermore, demonstration of an association between a candidate gene and BMD does not necessarily mean that the gene is causally responsible for the effect observed. Associations can also occur as the result of linkage disequilibrium with a causal gene situated nearby on the same chromosome. (See Ralston J Clin Endocrinol Metab. 87(6):2460-6 2002, Zajikova et al Endocr Regul. 37(1):31-44, 2003).

Furthermore, It is noted that patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable (*See Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966), Stating, in context of the utility requirement, that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."*) Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried

out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. Considering the state of the art which teaches that demonstration of an association between a candidate gene and BMD does not necessarily mean that the gene is causally responsible for the effect observed, the specification as filed fails to disclose that assessing the polymorphisms in any transmembrane signaling pathway gene along with any bone resorption gene is predictive of diagnosing any undesirable bone density condition (i.e. osteophorosis or high bone mass). The specification even fails to establish any bone density condition (i.e. osteophorosis or high bone mass) associated with all polymorphic gene associated with Vitamin D receptor and Interleukin-6 genes. The specification even fails to provide any evidence that establishes the association of any undesirable bone density conditions associated with the occurrence of a thymine residue 8 residues upstream of the normal start codon of the gene encoding vitamin D receptor and a cytosine residue at position -174 of the interleukin-6 gene promoter. Considering the instant specification it is even unclear how bone density is effected by the presence of these SNPs. The specification fails to provide any evidence, which establishes that assessment of these SNPs in combination would be a better predictor of assessing an undesirable bone density as compared to identification of a single SNP. The disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). The specification fails to enable one skill in the art to practice the invention as claimed without further undue amount of experimentation.

In instant case assessing any undesirable bone density conditions by genetic analysis of any trans-membrane signaling pathway gene along with any bone resorption gene is not considered routine in the art and without sufficient guidance to a specific genes of interest and a significant diagnostic value the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore considering the state of the art and limited amount of guidance provided in the instant specification, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to **571-272-0547.** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300.**

Sumesh Kaushal
Examiner GAU 1636

SUMESH KAUSHAL
PATENT EXAMINER